



General

Guideline Title

High blood pressure. In: Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents.

Bibliographic Source(s)

High blood pressure. In: Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents. Bethesda (MD): National Heart, Lung, and Blood Institute; 2011. p. 161-83. [23 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Definitions of the levels of the evidence (A, B, C, D) and strength of recommendations are presented at the end of the "Major Recommendations" field.

Note from the National Heart, Lung and Blood Institute (NHLBI) and the National Guideline Clearinghouse (NGC): Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents has been divided into individual summaries covering the major cardiovascular risk factors. In addition to the current summary, the following are available:

- [Family history of early atherosclerotic cardiovascular disease](#)
- [Nutrition and diet](#)
- [Physical activity](#)
- [Tobacco exposure](#)
- [Lipids and lipoproteins](#)
- [Overweight and obesity](#)
- [Diabetes mellitus and other conditions predisposing to the development of accelerated atherosclerosis](#)
- [Risk factor clustering and the metabolic syndrome](#)
- [Perinatal factors](#)

Conclusions of the Evidence Review 2003-2008

- The evidence review for the defined time period resulted in no major changes in the approach to blood pressure (BP) evaluation and management.

- In epidemiologic surveys of children and adolescents over the past 20 years, BP levels are increasing, and the prevalences of hypertension and prehypertension are increasing; these findings are explained partially by the rise in obesity.
- Prehypertension progresses to hypertension at the rate of approximately 7 percent per year; hypertension persists in almost one-third of boys and one-fourth of girls on 2-year longitudinal followup.
- From the evidence review, both breastfeeding and supplementation of formula with polyunsaturated fatty acid (PUFA) in infancy are associated with lower BP at followup.
- A DASH-style diet—which is rich in fruits, vegetables, low-fat or fat-free dairy products, whole grains, fish, poultry, beans, seeds, and nuts and lower in sweets and added sugars, fats, and red meats than the typical American diet—is associated with lower BP, as in adults. The Cardiovascular Health Integrated Lifestyle Diet (CHILD 1) combined with the Dietary Approaches to Stop Hypertension (DASH) eating plan (described in the NGC summary of [Nutrition and Diet](#)) is an appropriate diet for children that meets the DASH study and *Dietary Guidelines for Americans* 2010 (DGA) nutrient goals.
- Lower dietary sodium intake is associated with lower BP levels in infants, children, and adolescents.
- Losartan, amlodipine, felodipine, fosinopril, lisinopril, metoprolol, and valsartan can be added to the list of medications that are tolerated over short periods, and can reduce BP in children from ages 6 to 17 years but predominantly is effective in adolescents. For African American children, greater doses of fosinopril may be needed for effective BP control. Trial durations, however, were short, and long-term safety is still in question. Antihypertensive medications are shown in Table 8–5 in the original guideline document.
- In one study in small-for-gestational-age babies, a nutrient-enriched diet that promoted rapid weight gain was associated with higher BP on followup in late childhood. This potential risk should be considered when such diets are selected in the clinical setting.
- In one study, transcendental meditation has been shown to effectively lower BP in nonhypertensive adolescents.

Recommendations

Recommendations regarding BP are all graded as expert opinion (Grade D) since they are based on the expert consensus conclusions of *The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents*.

The current recommendations focus on a developmental approach to the prevention of cardiovascular disease (CVD) by appropriate identification and amelioration of risk factors during routine pediatric care. For BP, the *Fourth Report* provided an algorithm and flow diagram to assist clinicians in identifying hypertension in children. For these Guidelines, these recommendations are stratified to provide age-appropriate approaches that are congruent with the risk factor recommendations in other sections; this is reflected in Table 8–1 and in revised algorithms (see Figures 8–1 and 8–2 in the original guideline document). The BP norms for age, gender, and height are shown in Tables 8–3 and 8–4 in the original guideline document and are taken directly from the *Fourth Report*.

For children from birth to age 3 years:

- Routine measurement of BP is not recommended. Blood pressure should be measured when there is a suspicion of renal disease, coarctation of the aorta, or other condition that may be associated with BP elevation. Conditions under which children younger than age 3 years should have BP measured are listed in Table 8–2 in the original guideline document.
- In these young patients, auscultation of BP is often quite difficult, so measurement with an oscillometric device using an appropriate size cuff is acceptable. The state of the infant or young child (e.g., sleeping, quiet, fussing, crying) is very important in the interpretation of BP measurement.
- For younger patients, treatment of high BP is often directed at the underlying cause, since primary hypertension is uncommon.

For children, ages 3–11 years:

- Routine measurement of BP during health care visits is recommended. This is true of visits for health maintenance and for visits when the child is ill.
- Auscultation should be the method of choice for confirmation of elevated BP measurements using an oscillometric device. The BP percentiles from the *Fourth Report* based on age, gender, and height percentiles should be used to categorize BP as prehypertension or Stage 1 or Stage 2 Hypertension (see Tables 8–3 and 8–4 in the original guideline document). BP elevation must be persistent to be considered hypertension; the process for establishing the BP category is outlined in Table 8–1 and in Figures 8–1 and 8–2 in the original guideline document.
- In this age group, obesity is an increasingly important cause of BP elevation. When obesity is present, therapy should first be directed at improving diet and physical activity behaviors. This age group offers the opportunity to intervene early in the process of obesity development, allowing the clinician to focus on weight maintenance while the child grows, as opposed to weight loss. It also provides an important opportunity to introduce the DASH-style diet, which is described in the NGC summary [Nutrition and Diet](#), as an example of CHILD 1. The DASH diet focuses on increased fruits and vegetables, low-fat dairy products, and whole-grain foods and meets all nutrient and energy requirements for children in this age range. Dietary sodium intake should also be limited.

- BP category-specific management is outlined in Table 8–1 and Figure 8–2 in the original guideline document.

For adolescents, ages 12–17 years:

- The approach to the evaluation of BP is similar to that of children ages 3 to younger than 12 years, but the prevalence of primary hypertension is much more common, and obesity is a major concern as an underlying factor. As shown in Tables 8–3 and 8–4 in the original guideline document, the percentiles of the *Fourth Report* should be used to evaluate BP.
- Adolescents with obesity are at risk of type 2 diabetes mellitus. Diabetes is a condition for which more aggressive BP lowering is recommended; this is described in the NGC summary [Diabetes Mellitus and Other Conditions Predisposing to the Development of Accelerated Atherosclerosis](#), which addresses the management of children with high-risk conditions.
- In this age group, the level of BP indicating prehypertension is at least 120/80, the same as that for adults. This is because the 90th percentile for adolescents is higher than 120/80 for most ages and height percentiles.
- For adolescents with increased body mass index (BMI) and elevated BP, weight loss is the cornerstone of therapy. Both dietary and physical activity behaviors should be addressed, aiming for appropriate energy balance, lower dietary sodium, and a DASH-like dietary pattern. Recommendations for the management of obesity are outlined in the NGC summary [Overweight and Obesity](#).
- BP category-specific management is outlined in Figures 8–1 and 8–2 and in Table 8–1 in the original guideline document.

For young adults, ages 18–21 years:

- Adult cut points for BP in this age group are used to define hypertension, as per the *Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) guidelines*.
- In this age range, institution of the adult DASH diet is recommended for individuals with prehypertension or hypertension, as is reduction of dietary sodium. Overweight continues to be a major concern in this age group; weight reduction should be promoted through enhanced energy expenditure coupled with reduced energy intake. Physical activity should be promoted, since moderate-to-vigorous physical activity reduces BP levels in adults.
- The management of hypertension is as described in JNC 7.

For all age groups, the assessment of left ventricular mass (LVM) by echocardiography is recommended as the best method to assess hypertensive target organ disease. Assessment should be done for patients with stage 2 hypertension and those with persistent stage 1 hypertension. Evaluation of LVM may be helpful in establishing the need for pharmacologic treatment of hypertension.

Table 8–5 in the original guideline document shows medications that have been used to achieve BP control in children and adolescents. At present, no data support the use of specific antihypertensive agents for specific age groups, and long-term safety data are not available.

Age-Specific Recommendations for Blood Pressure (BP) Measurement and Diagnosis of Hypertension

BP recommendations are based on <i>The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents (Fourth Report)</i> *, with the evidence review updated from 2003.	
Recommendations are all graded as <i>expert opinion (Grade D)</i> as they are based on the expert consensus conclusions of the <i>Fourth Report</i> .*	
Birth–3 years	<p>No routine BP measurement</p> <ul style="list-style-type: none"> • Measure BP if history (+) for neonatal complications, congenital heart disease, urinary/renal abnormality, solid-organ transplant, malignancy, drug prescription or condition known to raise BP or increase intracranial pressure (see Table 8–2 in the original guideline document) <ul style="list-style-type: none"> • If BP at least 90th percentile by oscillometry, confirm by auscultation • If BP confirmed at least 90th percentile, initiate evaluation for etiology and treatment per algorithm. (See Figure 8–2 in the original guideline document.)
3–11 years	<p>Annual BP measurement in all, interpreted for age/sex/height per Tables 8–3 and 8–4 in the original guideline document:</p> <ul style="list-style-type: none"> • BP less than 90th percentile, repeat in 1 year • BP at least 90th percentile: <ul style="list-style-type: none"> Repeat BP × 2 by auscultation Average replicate measurements, then reevaluate BP category

	<p>→ If BP confirmed at least 90th percentile but less than 95th percentile = prehypertension (preHTN):</p> <ul style="list-style-type: none"> • Recommend weight management if indicated. • Repeat BP in 6 months. <p>→ If BP at least 95th percentile but less than 99th percentile + 5 mmHg:</p> <ul style="list-style-type: none"> • Repeat BP in 1–2 weeks, average all BP measurements. • Reevaluate BP category. • BP confirmed at least 95th percentile but less than 99th percentile + 5 mmHg = stage 1 HTN: <ul style="list-style-type: none"> • Basic work-up per Figure 8–2 in the original guideline document <p>→ If BP at least 99th percentile + 5 mmHg</p> <ul style="list-style-type: none"> • Repeat BP by auscultation × 3 <u>at that visit</u>, average all BP measurements. • Reevaluate BP category. • BP confirmed at least 99th percentile + 5 mmHg = stage 2 HTN: <ul style="list-style-type: none"> • Refer to pediatric HTN expert within 1 week <u>or</u> • Begin BP treatment and initiate basic work-up, per Figure 8–2 in the original guideline document.
12–17 years	<p>Annual BP measurement in all, interpreted for age/gender/height per Tables 8–3 and 8–4 in the original guideline document:</p> <ul style="list-style-type: none"> • BP less than 90th percentile, counsel on CHLD 1 diet, activity recommendations, and repeat BP in 1 year • BP at least 90th percentile <u>or</u> at least 120/80: <ul style="list-style-type: none"> • Repeat BP × 2 by auscultation • Average replicate measurements, then re-evaluate BP category <p>→ If BP confirmed at least 90th percentile but less than 95th percentile <u>or</u> at least 120/80 = preHTN:</p> <ul style="list-style-type: none"> • CHLD 1 diet, activity recommendations, weight management if indicated • Repeat BP in 6 months <p>→ If BP at least 95th percentile but less than 99th percentile + 5 mmHg:</p> <ul style="list-style-type: none"> • Repeat BP in 1–2 weeks, average all BP measurements. • Reevaluate BP category. • BP confirmed at least 95th percentile but less than 99th percentile + 5 mmHg = stage 1 HTN: <ul style="list-style-type: none"> • Basic work-up per Figure 8–2 in the original guideline document <p>→ If BP at least 99th percentile + 5 mmHg:</p> <ul style="list-style-type: none"> • Repeat BP by auscultation × 3 <u>at that visit</u>, average all BP measurements. • Reevaluate BP category. • BP confirmed at least 99th percentile + 5 mmHg = stage 2 HTN: <ul style="list-style-type: none"> • Refer to pediatric HTN expert within 1 week <u>or</u> • Begin BP treatment and initiate work-up, per Figure 8–2 in the original guideline document.
18–21 years	<p>Measure BP at all health care visits:</p> <ul style="list-style-type: none"> • BP at least 120/80 to 139/89 = preHTN • BP at least 140/90 to 159/99 = stage 1 HTN • BP at least 160/100 = stage 2 HTN <p>Evaluation/treatment per JNC recommendations**</p>

*High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 2004;114 (2 Suppl 4th Report): 555-76.

**Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ; National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 2003;21;289(19):2560-2572.

Definitions:

Evidence Quality for Grades of Evidence

Grade	Evidence
A	Well-designed randomized controlled trials or diagnostic studies performed on a population similar to the Guidelines' target population
B	Randomized controlled trials or diagnostic studies with minor limitations; genetic natural history studies; overwhelmingly consistent evidence from observational studies
C	Observational studies (case-control and cohort design)
D	Expert opinion, case reports, or reasoning from first principles (bench research or animal studies)

Guidelines' Definitions for Evidence-Based Statements

Statement Type	Definition	Implication
Strong recommendation	The Expert Panel believes that the benefits of the recommended approach clearly exceed the harms and that the quality of the supporting evidence is excellent (Grade A or B). In some clearly defined circumstances, strong recommendations may be made on the basis of lesser evidence (Grade C or D) when high-quality evidence is impossible to obtain and the anticipated benefits clearly outweigh the harms.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Recommendation	The Expert Panel believes that the benefits exceed the harms but the quality of the evidence is not as strong (Grade B or C). In some clearly defined circumstances, strong recommendations may be made on the basis of lesser evidence (Grade D) when high-quality evidence is impossible to obtain and the anticipated benefits clearly outweigh the harms.	Clinicians should generally follow a recommendation but remain alert to new information and sensitive to patient preferences.
Optional	Either the quality of the evidence that exists is suspect (Grade D) or well-performed studies (Grade A, B, or C) show little clear advantage to one approach versus another.	Clinicians should be flexible in their decision-making regarding appropriate practice, although they may set boundaries on alternatives; patient and family preferences should have a substantial influencing role.
No recommendation	There is both a lack of pertinent evidence (Grade D) and an unclear balance between benefits and harms.	Clinicians should not be constrained in their decision-making and should be alert to new published evidence that clarifies the balance of benefit versus harm; patient and family preferences should have a substantial influencing role.

Clinical Algorithm(s)

The following algorithms are provided in the original guideline document:

- Blood Pressure (BP) Measurement and Categorization

- Blood Pressure (BP) Management by Category

Scope

Disease/Condition(s)

- Atherosclerotic cardiovascular disease
- Cardiovascular health
- High blood pressure (hypertension, prehypertension)

Guideline Category

Diagnosis

Evaluation

Management

Prevention

Risk Assessment

Screening

Treatment

Clinical Specialty

Cardiology

Family Practice

Internal Medicine

Nursing

Nutrition

Pediatrics

Preventive Medicine

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Dietitians

Health Care Providers

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To provide comprehensive evidence-based guidelines addressing the known risk factors for cardiovascular disease (CVD)
- To assist all pediatric care providers in both the promotion of cardiovascular (CV) health and the identification and management of specific risk factors from infancy into young adulthood
- To provide recommendations to pediatric care providers on the evaluation and treatment of high blood pressure in their child and adolescent patients

Target Population

- Infants, children, and adolescents in the general population and their parents/guardians
- Children and adolescents with prehypertension or hypertension

Interventions and Practices Considered

1. Blood pressure measurement by auscultation or with an oscillometric device
2. Categorization of blood pressure as prehypertension or stage 1 or stage 2 hypertension using blood pressure percentiles based on age, gender, and height percentiles
3. Weight management if overweight or obesity is present
4. Use of a Dietary Approaches to Stop Hypertension (DASH)-style diet
5. Antihypertensive therapy

Major Outcomes Considered

- Incidence of high blood pressure in children and adolescence
- Systolic and diastolic blood pressure (in relation to diet, body mass index, lifestyle, and antihypertensive medication)

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Systematic Evidence Review

The foundation of the systematic evidence review performed in support of the guideline development process was a series of critical questions related to cardiovascular disease (CVD) risk and prevention in youth. The questions encompassed defined risk factors, predefined outcome measures for each risk factor, and, most importantly, measures of CVD and target organ damage (TOD). Each of these elements was developed and refined through a review of the existing evidence by the Expert Panel. Additional information on the Critical Questions can be found in Table A-1 in Appendix A of the original guideline document.

To inform the identification of studies related to the critical questions, the Expert Panel held an inservice training with the contractor staff members who would be involved in overseeing the literature review to initiate the evidence review process. In addition, a series of group training sessions was held with the contractor staff at appropriate points throughout the process to clarify the scope of the review and expectations for supporting the production of high-quality, evidence-based guidelines.

Search Parameters

Based on the critical questions, risk factors, and types of CVD TOD of interest, search parameters were developed to identify published studies relevant to pediatric cardiovascular (CV) risk reduction. This process involved determining appropriate databases, dates, terms, and limits for the search, as described below.

Databases

Searches were performed in the following databases:

- PubMed/MEDLINE
- Cochrane Database of Systematic Reviews
- National Guideline Clearinghouse (NGC)

Searches were first conducted in PubMed/MEDLINE. Only unique studies from subsequent searches in the Cochrane database and NGC were retained for consideration (i.e., those studies that were not already captured in the initial PubMed/MEDLINE search).

In addition to these databases, a preliminary search of EMBASE was conducted. The great majority of studies identified in this preliminary search were also found in the other databases; therefore, it was determined that proceeding with a complete EMBASE search would not contribute significant additional information to the review.

The literature search allowed for further input by the Expert Panel to ensure that in-scope studies were not overlooked. Members of the Expert Panel contributed additional relevant studies based on their routine scanning of the literature. A supplementary literature search was also conducted to identify potentially relevant studies authored by members of the Expert Panel. Additional studies identified by these supplementary methods were included only if they met the same criteria for inclusion established for the primary evidence review.

Search Dates

Original searches in PubMed/MEDLINE, Cochrane, and NGC captured studies published between January 1, 1985, and December 31, 2006. Recognizing the timelag inherent in screening a large body of literature and developing evidence tables, the Expert Panel then called for an update of these searches to be conducted for the period between January 1, 2007, and June 30, 2007.

The Expert Panel established June 30, 2007, as the closing publication date for literature to be entered into the evidence review for these Guidelines. The Expert Panel recognized that, given the scope of these Guidelines and the nature of ongoing research in relevant areas, research findings might appear thereafter with the potential to have a material impact on one or more recommendations in the Guidelines. Therefore, to optimize the currency of the Guidelines, the Expert Panel sought, prospectively, to enable consideration of directly relevant, significant peer-reviewed evidence that might appear after the closing date. During a conference call convened on January 21, 2008, the Expert Panel Science Team established the following criteria to guide the full Expert Panel's consideration of studies published after the closing date:

- Any peer-reviewed published study identified by a member of the Expert Panel, as part of his or her routine surveillance of the literature, that is directly relevant to the recommendations of the Expert Panel will be considered for inclusion.
- To be included by the Expert Panel as evidence, the corresponding Risk Factor Team, or the full Expert Panel if applicable at a broader level, must judge that the findings of such recently published studies have the potential for a material impact on the content or strength of the recommendations of the Expert Panel.
- Such studies must meet the same basic criteria for inclusion established for the primary evidence review.
- If there is a difference of opinion about inclusion of a study, a final decision will be made by the Expert Panel Chair.
- Studies that are selected for inclusion will undergo abstraction and full text review by the process established for the primary evidence review. To distinguish it from the body of evidence assembled via the systematic literature search conducted through the closing date of June 30, 2007, the body of evidence from any such more recent studies will be documented separately from the evidence tables comprising data from the original search.

Search Terms

To explore the most appropriate search strategy and examine the sensitivity and specificity of particular search terms, an initial search was done in PubMed/MEDLINE. This search used broad medical subject heading (MeSH) terms and text words for the concepts of pediatric/young adult populations, CVD/TOD, and the risk factors. Terms were combined using the Boolean operators "AND," "OR," and "NOT," which are described briefly in Table A-3 in Appendix A of the original guideline document.

The preliminary, broad search of PubMed/MEDLINE identified in excess of 1 million citations, signaling the need to refine the search terms to

identify the most relevant ones. In consultation with the Expert Panel, key refinements in the search strategy were made, including (1) the use of major MeSH terms rather than MeSH terms, where appropriate; (2) the use of title and abstract terms rather than text words; (3) a reduction of the number of terms for each concept, leaving only the most central and essential terms; and (4) the application of excluded concepts to the search (in the form of "NOT" terms).

In the final search strategy, a combination of MeSH terms, major MeSH terms, and title and abstract terms was employed to identify the full range of relevant literature. Search terms were identified to capture studies in the pediatric and young adult target populations (ages 0–21 years) that also addressed CVD/TOD and/or at least one of the risk factors. Specific search terms are provided in Table A–9 in Appendix A of the original guideline document.

Search Limits

A set of limits was applied to the search to help refine the results to the most useful types of studies. The first level of basic search limits included:

- *Publication date*: published between January 1, 1985, and June 30, 2007
- *Language*: English language abstract or full text
- *Publication type*: no editorials, letters, comments, case reports, or non-systematic reviews

Search terms and field tags used to apply these limits to the search are provided in Table A–9 in Appendix A of the original guideline document.

In addition to these basic limits, search terms were used to exclude studies examining certain out-of-scope conditions. For example, during a preliminary review of the literature, many studies were identified that focused on various pediatric conditions such as Kawasaki disease, otitis media, or congenital heart diagnoses. Through consultation with the Expert Panel, search terms were developed for the most commonly observed out-of-scope conditions. Studies containing these terms were prospectively excluded by using the Boolean operator "NOT."

Search Results

Systematic Reviews, Meta-Analyses, Randomized Controlled Trials, and the Guidelines

After applying the initial limits and using terms to eliminate out-of-scope concepts, the number of results returned from the original literature searches was still in excess of 60,000 citations. Given the size of these literature results, the Expert Panel determined that part of the review would focus on certain study types that would be most useful to the Expert Panel during Guidelines development: systematic reviews (SRs), meta-analyses (MAs), randomized controlled trials (RCTs), and guidelines. Search terms and field tags identifying study type were used to select these studies in the PubMed/MEDLINE database.

Secondary studies, such as SRs and MAs, compile results from primary analyses and, in some cases, review of these study types may lessen the need to examine primary evidence on a topic. However, given the breadth of this evidence review, there were no instances in which an SR or MA captured the entire scope of interest of a critical question; therefore, this review depended on RCTs as an important source of primary data on relevant interventions.

The schematic in Figure A–1 in Appendix A of the original guideline document presents a simplified, high-level depiction of how the key search concepts were combined to achieve the overall search strategy.

In childhood, much of the evidence linking risk factors to atherosclerosis comes from epidemiologic studies. Therefore, in addition to including SRs, MAs, RCTs, and guidelines in the review, the Expert Panel determined that it was necessary for the evidence review to include major epidemiologic studies selected by the Expert Panel. These studies represent landmark longitudinal and natural history studies and other sentinel work that have provided important information and insight about atherosclerosis and CV risk in children. The major observational studies that were included are listed in Table A–4 in Appendix A of the original guideline document.

A separate targeted search of PubMed/MEDLINE was conducted to identify literature relevant to these major studies related to the risk factors for the inclusive period of the evidence review from January 1, 1985, to June 30, 2007. The observational literature was also updated by the Expert Panel using the same criteria developed for the classic evidence review. Terms used to conduct this search are provided in Table A–10 in Appendix A of the original guideline document. National Heart, Lung and Blood Institute (NHLBI) staff reviewed the titles and then the abstracts for studies to be included based on the 14 risk factors under review. When a longitudinal study reported results of the same variables at increasing intervals from the beginning of the observational period, the most recent report detailing the longest period of observation was selected for inclusion. Duplicate reports of the same results were excluded. The observational studies to be included in the evidence review were selected by the Expert Panel Risk Factor Teams.

Additional References

In an evidence-based review, studies included are generally limited to RCTs, SRs, and MAs. In addition to the epidemiologic studies described above, Expert Panel members also included studies that provided important information for each risk factor, defining the context in which the Guidelines' recommendations were developed. These references are not part of the evidence tables but are identified sequentially throughout the text and will be listed in Appendix B of the original guideline document by section in numeric order, as identified in the text. Of particular importance were studies of genetic conditions impacting CV risk status and natural history studies of specific diseases known to be associated with accelerated atherogenesis.

Inclusion and Exclusion Criteria

In preparation for review of the literature, inclusion and exclusion criteria were developed by the Expert Panel. These criteria outlined additional boundaries for the review. Certain criteria were applied only by the Expert Panel, given that judgments regarding the application of these criteria required relevant clinical expertise.

Inclusion Criteria

- Pertained to at least one of the specified risk factors and measured at least one of the predetermined outcomes
- Related to at least one of the critical questions
- Focused on the target population (ages 0–21 years)
 - For longitudinal studies and other studies with extended followup periods, the population was required to be in this age range at initiation, and this subcohort could be identified in subsequent analyses.
 - For the Guidelines, the target population was required to include at least part of this age range.
- Conducted in Europe, North America, Australia, New Zealand, Japan, or Israel
- In 2004, an NHLBI-appointed Task Force published *The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents*. This report included a complete review of the current evidence on this subject and detailed recommendations for managing blood pressure (BP) throughout childhood. These recommendations were used as the basic recommendations for BP management for these Guidelines and are considered complete until 2003 when the review for the report ended. The literature review for BP, therefore, was limited to January 1, 2003, through June 30, 2007; selected studies from 2008 identified by the Expert Panel that met all the criteria for inclusion in the evidence review were also included.

Exclusion Criteria

- Any study not meeting the above requirements was excluded from the review.
- Studies that otherwise met inclusion criteria but that were found, upon examination, to have measured risk factors in only an incidental way or as part of assessing the safety of an intervention were excluded. For example, a study of an asthma medication might measure BP to ensure that there were no adverse effects of the medication. Such studies that measured in-scope outcomes that were not linked to a risk factor condition were excluded from the review.
- Duplicate reports of findings based on the same original studies were generally excluded. For instances in which a series of studies (typically longitudinal studies or large RCTs) reported results for the same outcome measures over a period of time, the most recent studies and main results of trials were typically retained and older studies were excluded. These determinations were made individually during the review of each study.
- Studies that did not meet basic internal/external validity standards (e.g., as a result of narrowly defined patient population) were excluded.
- Studies that addressed the target population, often as part of a broader age range, but did not provide findings specific to patients in the target age range were excluded.
- Studies were excluded that on closer inspection were found not to be SRs, MAs, RCTs, guidelines, or reports from the selected epidemiologic studies.
- Studies were excluded that had an insufficient number of patients at followup to draw meaningful conclusions.
- Studies conducted in patients with diabetes focused on interventions that were related exclusively to glycemic control were excluded.
- For studies that focused on smoking as a risk factor, those that reported on interventions related to policymaking or merchant behavior were excluded.

During the review process, inclusion and exclusion criteria were modified to account for topics identified as irrelevant and certain included topics were clarified. Throughout this process, abstractors and the Expert Panel were in close contact to resolve questions regarding the application of inclusion/exclusion criteria to individual studies.

Literature Review Process

After completing electronic searches in each database, a total of 11,231 SRs, MAs, RCTs, guidelines, and major observational studies were

identified for review. The distribution of search results by database and study type is presented in Table A–5 in Appendix A of the original guideline document.

Abstracts and citations for these studies were compiled and organized using Reference Manager.

Figure A–2 in Appendix A of the original guideline outlines the phases of the literature review process and the number of studies excluded at each stage. Throughout each review phase the Expert Panel provided guidance regarding the appropriate application of inclusion and exclusion criteria.

Following the review of titles and abstracts, trained abstractors conducted a full-text review of the studies and excluded additional studies. NHLBI staff also reviewed the full text of these studies and identified additional studies to exclude. Following the full-text review phase, an additional 200 studies were excluded. Citations for studies excluded at the full-text level are provided online, along with the complete evidence tables.

In addition to a review of the studies captured through the literature search process (i.e., studies published between January 1, 1985, and June 30, 2007), the NHLBI and the Expert Panel identified an additional 29 relevant studies that were published after June 30, 2007, for inclusion in the review.

Number of Source Documents

At the end of the review process, a total of 664 studies were included for review—including 51 systematic reviews, 34 meta-analyses, 304 randomized controlled trials (RCTs), 84 guidelines, and 191 observational studies.

The evidence review for the defined period (2003-2008) for this section on high blood pressure identified 9 observational studies, 13 RCTs, and 3 meta-analyses.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Evidence Quality for Grades of Evidence

Grade	Evidence
A	Well-designed randomized controlled trials or diagnostic studies performed on a population similar to the Guidelines' target population
B	Randomized controlled trials or diagnostic studies with minor limitations; genetic natural history studies; overwhelmingly consistent evidence from observational studies
C	Observational studies (case-control and cohort design)
D	Expert opinion, case reports, or reasoning from first principles (bench research or animal studies)

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data Collection and Quality Control

Systematic Reviews, Meta-Analyses, Randomized Controlled Trials, and Guidelines

To capture information from in-scope studies, Excel tables were developed and used for data abstraction of each study type (i.e., systematic review [SR], meta-analysis [MA], randomized controlled trial [RCT]). Through discussion the Expert Panel, the types of information collected and the format of the tables were refined. Data collected in the abstraction tables included basic information about the study (e.g., year of publication), objective, patient population, intervention and comparator/control (if applicable), outcomes measured, and results. Data abstracted varied by study type. A complete list of data fields and definitions for these fields is provided through the National Heart, Lung and Blood Institute (NHLBI) Web site.

To complete the data abstraction tables, trained abstractors reviewed full-text versions of each in-scope study. Two reviewers examined each full-text study; the first reviewer abstracted the appropriate data from each study, while the second reviewer concentrated on ensuring the accuracy and quality of data entered by the first reviewer as part of a thorough quality control process. For RCTs, contractor staff abstracted information for specific columns, including basic information about the study, objective, patient population, intervention and comparator/control (if applicable), and outcomes measured. For SRs and MAs, the contractor staff abstracted information for all columns. For observational studies, contractor staff abstracted the basic informational data, but full-text review and data entry were performed by NHLBI staff.

After data abstraction by the contractor, the data abstraction tables were submitted to the NHLBI and the Expert Panel for review and/or completion of abstraction. For all study types, Expert Panel members were responsible for verifying data entered by the contractor. For RCTs, Expert Panel members and NHLBI staff selected the outcome variables to be abstracted and entered the results in the evidence tables, as well as recorded study results and conclusions. To facilitate this process, studies were forwarded to the relevant subcommittee within the Expert Panel, according to the primary risk factor of focus. For example, a study that examined the use of an intervention to improve cholesterol levels would have been forwarded to the subcommittee on lipids. Study reviews were rotated to ensure that each was reviewed by two subcommittee members. Subcommittee members completed abstraction of established columns and, in several cases, requested the addition of extra columns in the evidence tables to capture more specific information pertaining to the risk factor of interest. When Expert Panel members were not in agreement regarding such matters as study relevance or abstraction of specific data, these matters were brought to the Expert Panel Chair for resolution.

In addition to basic information about study design and results, aspects of study quality were considered by the Expert Panel during data abstraction. A customized quality grading system was developed to support the Expert Panel's interpretation of individual studies, particularly with regard to methodology and study design considerations. This novel grading system, the development of which drew largely from several existing grading schemes, was incorporated into the electronic data abstraction tables. The system used an algorithm that generated a quality grade for individual RCTs, according to the criteria outlined in Tables 11 and 12 in Appendix A of the original guideline document. SRs, MAs, and observational studies did not receive an individual quality grade.

After completion of data abstraction, evidence tables displaying key study information were developed from the data abstraction tables using Excel for use by the Expert Panel. These standard evidence tables were then sorted in a customized way for each subcommittee, so as to best support the Guidelines development process. Final evidence tables for all included SRs, MAs, RCTs, and observational studies are provided online at http://www.nhlbi.nih.gov/guidelines/cvd_ped/index.htm .

Although reports of guidelines were captured as part of the literature search, they were not incorporated into evidence tables. Instead, the guidelines were reviewed for relevance, and those that were in scope were categorized according to the risk factor(s) addressed. A list of the in-scope guidelines was made available to Expert Panel members for their reference; full-text versions were made available as needed. Citations for in-scope guidelines, by risk factor, are also provided online.

Major Observational Studies

Excel tables were also developed for the epidemiologic observational studies, with basic information about each study entered into tables by skilled abstractors from contractor staff. Full-text review and abstraction of each study were performed by NHLBI staff, including identification of outcome variables and review of results and conclusions. These tables were then reviewed by Expert Panel members, who selected 191 studies as relevant to the evidence review. The tables were primarily categorized by risk factor and then sorted using the terms developed by the relevant Risk Factor Teams for inclusion in the review. Expert Panel members added additional relevant reports from any of these observational studies that appeared after conclusion of the formal review. The evidence tables for the observational studies are also included on the NHLBI Web site.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Expert Panel and Subcommittee Discussion

Following establishment of the Expert Panel, in-person meetings were held in October 2006, February 2007, June 2008, and October 2008. These meetings enabled Expert Panel members to discuss key elements of the systematic evidence review, consider the approach and scope of the Guidelines, and review and refine the Guidelines' recommendations.

To facilitate discussion of the evidence related to particular risk factors, multiple subcommittee conference calls were held from February to December 2008, along with a continuous electronic correspondence. Across the seven subcommittees, more than 500 conference calls were completed. During these calls, subcommittee members established processes for developing and finalizing the Guidelines' recommendations for each risk factor and progressively shaped the final recommendations in the Guidelines. A SharePoint Web site was created to enable subcommittee members to share draft recommendations.

Established Parameters for Guidelines Recommendation Development

The Expert Panel adopted an evidence grading system from the American Academy of Pediatrics (AAP) to assess the quality of the body of evidence as a whole and the evidence in support of particular statements. The grading system is shown in the "Rating Scheme for the Strength of the Evidence" field; it was modified by the addition of genetic natural history studies to the grade B evidence category; an example of a genetic natural history study is the development of atherosclerosis in a child with homozygous familial hypercholesterolemia who has severely elevated cholesterol levels from birth. Studies of such genetic conditions are believed to represent a natural intervention and to function as surrogates for a specific lifelong risk exposure. Genetic variation shares features with random assignment in clinical trials in that the variation occurs by chance within a society and the presence of the genetic variation does not alter exposure to environmental or other factors. Drawing from the same AAP system, the "Rating Scheme for the Strength of the Recommendations" field depicts the Guidelines' definitions for evidence-based statements.

The Expert Panel also developed a definition of consensus to guide decision making regarding Guidelines recommendations within the subcommittees and among the full Expert Panel. The final definition included the following elements:

- Committee deliberations regarding a given recommendation generally reflected deference to the expert risk factor subcommittee that was originally charged with critically appraising the evidence and drafting the recommendation.
- Voting was "in support of" or "opposed to" a recommendation.
- Agreement by at least 80 percent (or 11 of 14 members) of the Expert Panel constituted a strong consensus. A recommendation with this level of agreement is presented in the Guidelines as a consensus of the Expert Panel. However, discussion of the issues in the Guidelines document may address areas of difference.
- A proposed recommendation that was supported by less than 60 percent (or less than 8 of 14 members) of the Expert Panel was not included in the Guidelines. However, review of the subject could be included in the discussion for that risk factor area.
- Agreement by 60–80 percent (9 or 10 of 14 members) of the Expert Panel constituted a moderate consensus in support of the recommendation. A recommendation with this level of agreement was presented with that language in the Guidelines and accompanied by discussion of the conflicting issues. In developing the discussion in support of a recommendation, the actual vote of the Expert Panel was considered.

In considering the various pediatric age groups covered by the Guidelines' recommendations, the Expert Panel agreed to formulate the Guidelines' recommendations according to the chronological timetable used by the AAP *Bright Futures* program:

- Preconception/prenatal
- 0–12 months
- 1–4 years
- 5–10 years
- 11–17 years
- 18–21 years

Studies were not always specific to an age group, and the Expert Panel used judgment in determining how those studies informed age-specific recommendations.

Completion of the Guidelines

At the final full Expert Panel meeting in October 2008, the Expert Panel reviewed each recommendation proposed by each subcommittee in detail. According to the established definition of consensus, the Expert Panel agreed on a complete set of recommendations and supporting text in the

Rating Scheme for the Strength of the Recommendations

Guidelines' Definitions for Evidence-Based Statements

Statement Type	Definition	Implication
Strong recommendation	The Expert Panel believes that the benefits of the recommended approach clearly exceed the harms and that the quality of the supporting evidence is excellent (Grade A or B). In some clearly defined circumstances, strong recommendations may be made on the basis of lesser evidence (Grade C or D) when high-quality evidence is impossible to obtain and the anticipated benefits clearly outweigh the harms.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Recommendation	The Expert Panel believes that the benefits exceed the harms but the quality of the evidence is not as strong (Grade B or C). In some clearly defined circumstances, strong recommendations may be made on the basis of lesser evidence (Grade D) when high-quality evidence is impossible to obtain and the anticipated benefits clearly outweigh the harms.	Clinicians should generally follow a recommendation but remain alert to new information and sensitive to patient preferences.
Optional	Either the quality of the evidence that exists is suspect (Grade D) or well-performed studies (Grade A, B, or C) show little clear advantage to one approach versus another.	Clinicians should be flexible in their decision-making regarding appropriate practice, although they may set boundaries on alternatives; patient and family preferences should have a substantial influencing role.
No recommendation	There is both a lack of pertinent evidence (Grade D) and an unclear balance between benefits and harms.	Clinicians should not be constrained in their decision-making and should be alert to new published evidence that clarifies the balance of benefit versus harm; patient and family preferences should have a substantial influencing role.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

In April 2009, a draft version of the Guidelines was circulated to other National Institutes of Health (NIH) Agencies and multiple professional organizations for review and comment. The draft version was also posted on the National Heart, Lung and Blood Institute (NHLBI) Web site for public comment for a 30-day period from June 19 to July 20, 2009. In total, the Expert Panel considered more than 1,000 comments from more than 50 reviewers, and individual responses were developed for more than 1,000 comments. The draft version of the Guidelines also underwent a separate review by the NHLBI and the U.S. Department of Health and Human Services (HHS). After considering all comments, consistent with applicable Federal requirements, the Expert Panel made appropriate revisions to the draft report. The summary report was published in final form November 11, 2011.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

The promotion of cardiovascular (CV) health and the identification and management of specific risk factors (e.g., high blood pressure) from infancy into young adult life

Potential Harms

Refer to Table 8–5 in the original guideline document for cautions and adverse effects of antihypertensive medication use.

Contraindications

Contraindications

Refer to Table 8–5 in the original guideline document for contraindications of specific antihypertensive medications used in the pediatric population.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Clinical Algorithm

Patient Resources

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

High blood pressure. In: Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents. Bethesda (MD): National Heart, Lung, and Blood Institute; 2011. p. 161-83. [23 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011

Guideline Developer(s)

National Heart, Lung, and Blood Institute (U.S.) - Federal Government Agency [U.S.]

Source(s) of Funding

United States Government

Guideline Committee

Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents

Composition of Group That Authored the Guideline

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Refer to the original guideline document for members of the National Heart, Lung, and Blood Institute staff and for names of the contractor support.

Financial Disclosures/Conflicts of Interest

Expert panel members disclosed relevant financial interests to each other prior to discussions. The following financial interests are reported in the publication in the *Journal of Pediatrics*:

Dr. Benuck, Dr. Christakis, Dr. Dennison, Dr. O'Donnell, Dr. Rocchini, and Dr. Washington have declared no relevant relationships.

Dr. Daniels has served as a consultant for Abbott Laboratories and Merck, Schering-Plough. He has received funding/grant support for research from the NIH.

Dr. Gidding has served as a consultant for Merck, Schering-Plough. He has received funding/grant support for research from GlaxoSmithKline.

Dr. Gillman has given invited talks for Nestle Nutrition Institute and Danone. He has received funding/grant support for research from Mead Johnson, Sanofi-aventis and the NIH.

Dr. Gottesman has served on the Health Advisory Board, Child Development Council of Franklin County. She was a consultant to Early Head Start for Region 5B. She has written for iVillage and taught classes through Garrison Associates for the State of Ohio, Bureau of Early Intervention Services and Help Me Grow program. She has received funding/grant support for research from NIH.

Dr. Kwitrovich has served as a consultant or advisory board member for Merck, Schering-Plough, Pfizer, Sankyo, LipoScience and AstraZeneca. He has served on speaker bureaus for Merck, Schering-Plough, Pfizer, Sankyo, Kos and AstraZeneca. He has received funding/grant support for research from Pfizer, Merck, GlaxoSmithKline, Sankyo and Schering-Plough.

Dr. McBride has served as a consultant or advisory board member for Bristol-Myers Squibb, and Merck. He has served on speakers bureaus for Kos, Merck and Pfizer. He declared no relevant relationships since July 2007.

Dr. McCrindle has been a consultant for Abbott, Bristol-Myers Squibb, Daichi Sankyo and Roche. He owns stock in CellAegis. He reports funding/grant support for research from AstraZeneca, Sankyo, Merck, Schering-Plough and the NIH.

Dr. Urbina reports funding/grant support for research from Merck, Schering-Plough, Sankyo and the NIH.

Dr. Van Horn has provided advice to Chartwells School Food Service. She has received funding/grant support for research from General Mills and the NIH.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the [National Heart, Lung, and Blood Institute \(NHLBI\) Web site](#) .

Print copies: Available from the NHLBI Information Center, P.O. Box 30105, Bethesda, MD 20824-0105; e-mail: nhlbic@dgsys.com

Availability of Companion Documents

The following are available:

- Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents. Summary report 2011.

Bethesda (MD): National Heart, Lung, and Blood Institute; 2011. 125 p. Electronic copies: Available in Portable Document Format (PDF) from the [National Heart, Lung, and Blood Institute Web site](#) .

- Evidence tables. Electronic copies: Available in PDF from the [National Heart, Lung, and Blood Institute Web site](#) .

Patient Resources

Various resources for the public about heart and vascular diseases are available from the [National Heart, Lung and Blood Institute Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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